REMARKS

Claims 1 – 5, 7 – 12, 14, and 16 are currently pending. Of these, Claims 1 and 2 are the pending independent claims.

In the Office Action, Claims 1 – 5, 7 – 12, 14, and 16 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. In addition, Claims 1-5, 7, 8, 11, 12, and 14 were rejected under 35 U.S.C. § 103(a) as allegedly obvious from U.S. Patent No. 5,508,044 to Buxton ("Buxton") combined with Cervenakov et al. (International Urology and Nephrology, 34, 25-29, 2002) ("Cervenakov"), Jan et al. (Chinese Journal of Physiology, 4(14), 181-188, 1998) ("Jan"), and U.S. Patent No. 6,602,522 to Chen et al. ("Chen"). Claims 9 and 10 were also rejected under 35 U.S.C. § 103(a) as allegedly obvious from Buxton combined with Cervenakov, Jan, and Chen.

Finally, the Office Action indicated that priority to the original Slovenian application is denied because no English translation of the Slovenia P-200300317 document has been provided.

Each of the foregoing rejections is respectfully traversed. Favorable reconsideration is requested in view of the above amendments and following remarks.

I. The Slovenian Priority Application.

In regard to the claim of foreign priority to Slovenian application P-200300317, Applicants are in the process of having an English language translation prepared. As soon as the translation is available, Applicants will forward it to the Examiner.

II. The Indefiniteness Rejections.

The Examiner contends Claims 1 – 5, 7 – 12, 14, and 16 are indefinite in two respects. First, he contends the limitation "providing a lower biological variability" in Claim 1 is vague and indefinite. In response, Applicants have deleted this limitation from Claim 1, without prejudice. The Examiner also argues that Claim 16 is indefinite because it depends from now cancelled Claim 13. In response, Applicants have amended Claim 16 to depend instead on Claim 1.

In view of the aforementioned amendments, it is submitted that all indefiniteness rejections have been overcome and should now be withdrawn.

III. The Obviousness Rejections.

Finally, the Examiner contends Claims 1 and 2, and each of their dependent claims, would have been obvious over Buxton in combination with Cervenakov, Jan, and Chen. It is respectfully submitted that these rejections are not well taken. It has not been shown that a person of skill, unaware of Applicants' claimed invention, would have had any basis under the law of obviousness to combine the noted portions of Buxton, Cervenakov, Jan, and Chen in a manner which would have provided the invention as claimed.

Applicants first note the Examiner's designation of Buxton as the "primary" reference in the combination. Applicants do not wish to quibble over semantics or labels, but they are at a loss to see how Buxton could be a central or "coalescence" point for this collection of references. Buxton is directed to formulations which *combine diltiazem with hydrochlorothiazide*. Buxton mentions nothing in regard to tamsulosin, the active ingredient specified in the present claims. In contrast, Applicants' claims are directed to tamsulosin formulations. Tamsulosin is a selective alpha-one receptor antagonist known to be effective for a condition called "benign prostatic upperplasia." These drugs are completely unrelated to one another, and it has not been shown how or why a person of skill considering ways to improve tamsulosin formulations would have any reason to look to a patent like Buxton which describes a diltiazem/ hydrochlorothiazide combo drug which aims to provide for slow release of the blood pressure/ angina heart medicine diltiazem and immediate release of the diuretic ("water" pill) medicine hydrochlorothiazide in one tablet, pill, capsule, or the like for what is said to be "additive" effects for better treatment of high blood pressure conditions.

Nonetheless, the Examiner argues that Buxton might be modified to include tamsulosin, along with diltiazem in view of the teachings of Cervenakov and Jan. According to the Examiner Cervenakov teaches that tamsulosin may be used in the treatment of kidney stones while Jan teaches that diltiazem (disclosed in Buxton) may also be used in treatment of kidney stones. Therefore, the Examiner posits that it would have been obvious to combine the diltiazem of Buxton with the tamsulosin disclosed in Cervenakov in a single formulation for the treatment of kidney stones.

This purported combination fails, however, because it ignores the complete teachings of Buxton and also ignores that possibility (or even likelihood) of adverse side effects which might result from the proposed combination of drugs.

In particular, the Examiner ignores that fact that Buxton is not directed to a formulation for diltiazem by itself but to a formulation which *combines diltiazem with hydrochlorothiazide*. Diltiazem is a medication used to treat both hypertension and heart arrhythmias. In addition, hydrochlorothiazide is also used to treat hypertension and in some instances to treat and/or prevent kidney stones. Thus, the Buxton formulation already includes two anti-hypertension drugs.

The Examiner now proposes to add tamsulosin to the mix. As the Examiner knows, tamsulosin is typically used for prostatic hyperplasia and sometimes for passage of kidney stones. While tamsulosin is not prescribed for hypertension, it is known to cause hypotension or low blood pressure as a side effect. Thus, the Examiner proposes to combine three different blood pressure reducing medications in a single formulation.

One of ordinary skill in the art would not cavalierly modify the Buxton reference in this manner. Those of skill in the pharmaceutical arts clearly recognize that too much of a good thing can be quite harmful. In this case, the Buxton formulation already includes a potent combination of two blood pressure reducing agents. One of skill in the art would recognize that the further addition of tamsulosin to this mixture likely result in a formulation containing a dangerous excess of blood pressure reducing agents. Usage of such a formulation would create a substantial risk of hypotension in the patient.

For at least this reason, the Examiner's purported combination of prior art references fails to suggest the subject matter of the present claims.

Moreover, both Claims 1 and 2 are amended herein to specify that the pellet core comprises microcrystalline cellulose, in an amount from about 75 to about 90 weight percent of the pellet core in addition to tamsulosin or a pharmaceutically acceptable salt thereof and at least one water insoluble permeable polymer. None of the cited references, whether considered individual or in combination with one another, suggests this aspect of the presently claimed invention.

Buxton, the Examiner's primary reference, fails to disclose or suggest microcrystalline cellulose, in an amount from about 75 to about 90 weight percent in a pellet core. According to

Buxton, the amount of microcrystalline cellulose spheronizing agent should be limited to at most 60% and more preferably from about 15% to about 40% by weight of the core. *See* Col. 3, lines 36 – 39. The amount of microcrystalline cellulose must be limited because, according to Buxton, the bead or core the "beads preferably contain between 40% and 98%, more preferably between 60% and 85%, especially between 70% and 85% by weight" of the pharmaceutically active ingredient (diltiazem, since once again Buxton fails to disclose anything in regard to tamsulosin). *See* Col. 3, lines 22 – 25. Thus, the Examiner cannot rely on Buxton as disclosing this limitation in the current claims.

Turning to the supporting references, neither the Cervenakov reference nor the Jan reference says anything in regard to the use of microcrystalline cellulose. In fact, neither reference says anything at all in regard to the use of any form of excipients. Thus, neither Cervenakov nor Jan can overcome the aforementioned deficiencies in the primary reference, Buxton, and citation to the Cervenakov and Jan references fails to meet the Examiner's burden of demonstrating that the microcrystalline cellulose limitation would have been obvious to a person of ordinary skill in the art.

Finally, the Chen reference discusses the use of microcrystalline cellulose as a filler. Chen, however, instructs that the amount of this filler should be limited to about 20 to 50 wt%, and more preferably about 25 to 40 wt% of the granulation. *See* Col. 3, lines 34 – 40. Thus, Chen also fails to disclose or suggest a pellet core comprising in an amount from about 75 to about 90 weight percent of the pellet core.

In light of the foregoing, it is clear that the Examiner has failed to carry his burden to demonstrate that each and every limitation of the present claims is disclosed or suggested by the purported prior art combination of the Buxton, Cervenakov, Jan, and Chen references. Accordingly, Applicants respectfully request the Examiner reconsider the application, withdraw the rejections, and issue a notice of allowance at the earliest possible convenience.

In the event this response is not timely filed, the Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,
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